II

ON ULCERATING GRANULOMA OF THE PUDENDA

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SYNONYMS. GRANULOMA VENEREUM. GRANULOMA INGUINALE

ULCERATING granuloma of the pudenda is a disease of tropical origin; it is also a venereal disease, for it is acquired in copula. It is rarely seen in England, so that opportunities of observing this most intractable condition seldom arise, though it is common in India, China, West Africa, throughout South America, and the West Indies, in Papua and Northern Australia. The disease occurs in both sexes and in all races.

To G. Vianna, of Brazil (1913), we are indebted for the introduction of intravenous medication with tartar emetic in the treatment of this granuloma; and success in this direction at a later date led to the application of this drug to kala-azar and other tropical diseases. Granuloma pudendi is therefore of historic importance.

From time to time doubts have been expressed whether antimony tartrate is as effective in ulcerating granuloma as it at first appeared to be, for both the exact amount of the drug necessary, and the period over which it must be given to produce a cure, vary greatly.

Araujo [1] in his exhaustive monograph on this disease recommended intravenous injection, combined with local application of antimony; the sores, he thinks, should be treated directly twice daily with a 1 per cent. solution of tartar emetic in physiological saline solution.

During recent years very few papers on this subject have appeared; beyond recording the cure of the disease, few state explicitly the amount of the drug actually used to bring about that cure. Henry [2] has abandoned the local application of 1 per cent. tartar emetic as being too

painful; Schochet [3] and Lynch [4] refer solely to the intravenous method of medication; and Onorato considers that the best results are obtained in combination with X-rays.

Randall [5] has reported favourably on the injection of triamide of antimony thioglycollic acid (T.A.T.) and sodium antimony thioglycollate (S.A.T.).

Etiology and Pathology.—Many parasites have been described in ulcerating granuloma, but none of them has been generally accepted. Bodies, thought to be parasitic, have been described by Donovan [6] as short bacilli with rounded ends. These and the diplococcal organisms of Aragao [7] and Vianna, now known as *Calymmatobacterium granulomatis* (or *B. mucosus capsulatus*, Walker), are probably one and the same organism. We have seen similar organisms in surface scrapings of the ulcers in our cases, but regard them as merely surface contaminations. In sections of the growing edge of the lesions we have entirely failed to find any of these organisms in the deeper layers. We are therefore of the opinion that the causal organism of ulcerating granuloma still remains to be discovered.

Histology.—The structure of ulcerating granuloma is said to resemble that of rhinoscleroma very closely. That the latter disease is thought to be due to a bacterium —*B. rhinoscleromatis*—is well known. Snijders [8] has lately drawn attention to the occurrence of rhinoscleroma in Sumatra, and has suggested that it and granuloma pudendi may have a similar etiology.

Macleod [9] has described the structure as that of a typical granuloma, with essentially a thickening of the epidermis and elongation of the interpapillary processes.

Fig. 1 represents diagrammatically the structure of the growing edge of the granuloma such as we have observed it. The chief features to which we draw attention are the occurrence of islands or cell nests of the Malpighian layer within the main stratum itself, or buried deep in the tissues of the corium. At the margins of the lesions there are pyknotic changes in the nuclei of the Malpighian cells and evidences of active division in the deeper layers. The corium itself is infiltrated with round and plasma cells.

The evidence obtained from a histological study suggests a subacute or chronic type of inflammation, due to

an organism of comparatively low virulence. This, in the main, agrees with the description of the pathology given by Araujo.[10]

In the account that follows of the five cases which we

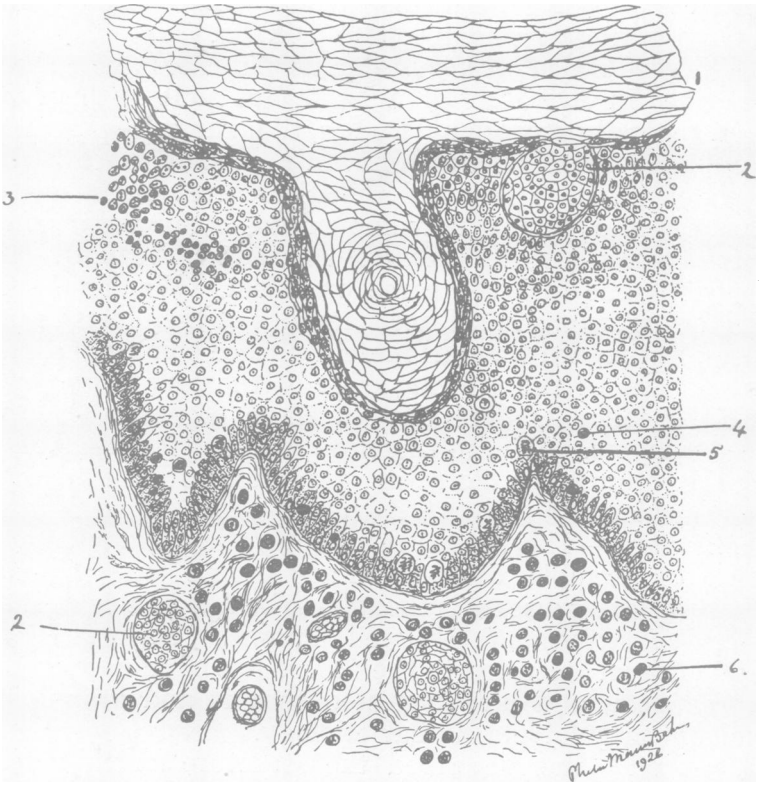


FIG. 1.—ULCERATING GRANULOMA OF THE PUDENDA.

Section through the edge of lesion showing characteristic pathological changes.

1. Stratified epithelium.
2. Cell nests and inclusions formed of cells of Malpighian layer.
3. Chromatolysis of nuclei of cells of Malpighian layer.
4. Infiltration of round cells into Malpighian layer.
5. Active mitosis of nuclei.
6. Infiltration of corium with round cells and plasma cells.

have observed and treated during the last four years, we wish to lay stress upon the variable manner in which the several cases responded to treatment, and the necessity of local treatment with antimony ointment in refractory cases. Antimony injections must be continued until firm scarring of the ulcerated surface has taken place. Atten-

tion is also drawn to the satisfactory results obtained with organic compounds of antimony, more especially Von Heyden, 471 (Meta-chlor-para-acetyl-amino-phenyl stibiate of sodium.)

In order to demonstrate the great variability in the

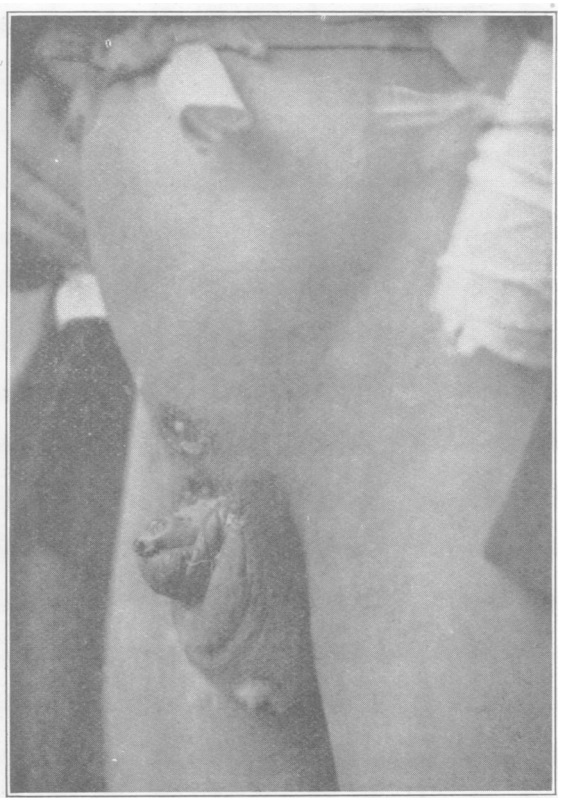


Photo by P. Kilner, Esq., F.R.C.S.

I.

CASE I.—ULCERATING GRANULOMA.

Shows destruction of dorsum of penis and contact inoculation lesions on the anterior abdominal wall.

clinical picture and in the extent of the lesions and their response to treatment, we append a short protocol of each of these five cases.

Case I (*Photograph* I).—A white European sailor, aged thirty-nine years, contracted ulcerating granuloma in Hong Kong in August, 1921. Seven days after coitus there appeared a small pimple on the corona glandis,

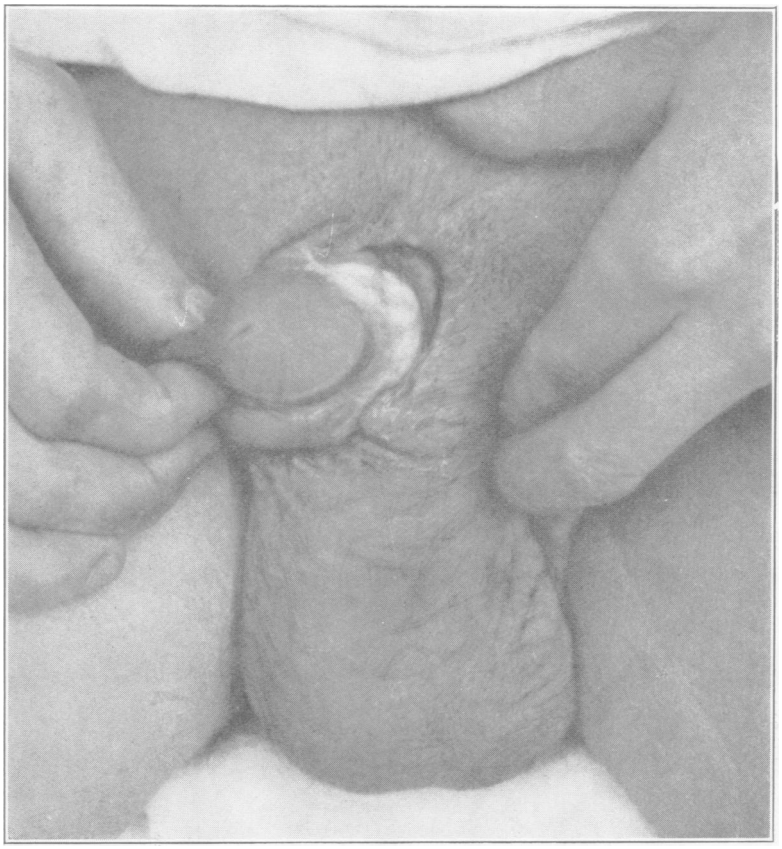
which three days later broke down to become an ulcer, which spread, undermining the dorsum of the glans penis. One month later he came under medical observation, and was treated for over one year as suffering from some form of syphilitic ulceration, receiving many injections of salvarsan, together with mercury inunctions and potassium iodide (many blood tests proving always Wassermann negative). The ulcer was scraped, and at one time partially removed by operation, but without checking its onward spread. Ulceration invaded both groins and the anterior surface of the abdomen, where, by undermining, it caused considerable destruction of tissue. When he came under our care in the Albert Dock Hospital, besides the groin ulcers there was deep ulceration of skin at the root and on the dorsum of the penis; it had burrowed under the skin of symphysis pubis to the depth of 1 inch, and such was the destruction of the glans penis that the organ could be recognised only by a stump with urethral opening at its extremity.

Treatment with antimony tartrate (potassium antimony tartrate) by intravenous injection was commenced in October, 1922, and continued with minor interruptions till March, 1925 (a period of two and a half years), when complete healing by sound scar tissue had taken place. He received 179 grains of antimony tartrate intravenously, commencing with a dose of $\frac{1}{2}$ grain and increasing by bi-weekly injections to $2\frac{1}{2}$ grains for a single dose. In addition, he received by intramuscular injection sixty-four treatments of oscol stibium (a colloidal preparation of antimony—Oppenheimer).

In November, 1922, the penile lesion having healed, the ulcerated area on abdomen was excised, and the wound covered by healthy skin. For seven days this appeared to have been successful, but soon after that it all broke down again. For the last year of treatment, local inunction by antimony ointment was adopted, and proved eminently successful as a means of healing up outstanding indolent ulcerations which hitherto had shown no sign of healing up. Tabloids of thyroid extract were given as an accessory, and appeared to promote healing.

Case 2.—A white trader, aged thirty-one years, from West Africa, was admitted to the Albert Dock Hospital in November, 1923, with an ulcerating granuloma, situate

on the pubes. The ulcer had appeared seven days after coitus on the Gold Coast, and had gradually extended till three months later it had reached the size of a half-crown piece. His blood was Wassermann negative. In this instance the intravenous injection of antimony



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II.

CASE 4.—ULCERATING GRANULOMA.

Showing extension round the base of the penis and invasion of the suprapubic fat.

tartrate had an almost instantaneous effect, and he was discharged with healed firm durable scar after one month, in which time he had received a total of 17½ grains.

Case 3.—A white trader, aged thirty-three years, contracted ulcerating granuloma in Capetown in June, 1922. It appeared as a pimple on the glans penis six days after

coitus. The papule soon broke down and became an open ulcer about the size of a threepenny bit. On his return to England, at the latter end of 1922, the sore involved all the dorsum of the penis, isolating an œdema-

Original Photo.

III.

CASE 5.—ULCERATING GRANULOMA.

tous mass at the frænum. There was a deep ulcer-trench round the root of the penis, encircling the whole organ with a ring of granulation tissue; ulceration had not spread on to the anterior abdominal wall. Blood Wassermann negative.

Treatment lasted six weeks at the Albert Dock Hospital, during which time he received 40 grains of potassium antimony tartrate intravenously. The response to antimony in this case was remarkable, proliferation of

Original Photo.

IV.

CASE 5.—ULCERATING GRANULOMA.

Showing firm scar tissue formation after treatment with antimony tartrate.

epithelium over the ulcer becoming apparent almost immediately.

Case 4 (*Photograph* 2).—A Chinaman, about thirty years of age, admitted to the Albert Dock Hospital in March, 1925. Apparently his lesion had been present for over a year already. The disease had been contracted in Shanghai. The glans penis itself had escaped. Ulceration extended in ring fashion round the root of the organ and undermined the tissues of the pubes. It exuded an

acid and peculiarly malodorous discharge, which we consider to be characteristic of the condition. There was no involvement of the lymphatic glands. His blood was Wassermann negative.

Treatment lasted for six months, during which time he received 106 grains of potassium antimony tartrate intravenously, and local healing was stimulated by application of 1 per cent. antimony tartrate ointment. A firm, durable scar resulted.

Case 5 (*Photograph* 3).—A white sailor, aged 21 years, contracted ulcerating granuloma in Trinidad. Some twelve weeks after coitus a sore appeared on his left groin, which gradually grew till it reached 1½ inches in length. Three other contiguous sores appeared as if inoculated by immediate contact. The oozing surface in this case discharged a clear, characteristically malodorous fluid. His blood was Wassermann negative.

During his two months' treatment in the hospital for tropical diseases he received in all 3 gm. of Von Heyden 471 intravenously, commencing with 0·1 gm. twice weekly, gradually increasing to 0·2 gm. three times weekly. In this case marked benefit seemed to accrue from the local application of antimony ointment.

Healing by firm scar tissue (Photo 4) took place.

We now propose to summarise the information we have obtained from a study of these five cases.

(1) When the lesion appears on the penis, the incubation period is, as is generally stated, about six to eight days after sexual contact; but with an extra-genital lesion, incubation may be as long as twelve weeks. (Case 5).

(2) The characteristic method of spread is by the gradual undermining of sound tissue at the growing edge, while healing by proliferation of epithelium over the surface takes place immediately behind it. Spread by actual contact inoculation may occur, thus bringing about multiple ulceration as in cases No. 1 and 5.

(3) There is no evidence that the lymphatic glands draining the area are ever permanently involved, though they may become enlarged from secondary septic infection. Fresh extension of ulceration to fresh areas of skin are invariably heralded by a very considerable amount of pain.

(4) The Wassermann reaction in these cases was invariably negative.

(5) The ulceration may burrow deeply into the subcutaneous tissue forming deep fistulæ, and, as had occurred in one case we saw, who was admitted to hospital moribund, a fistulous opening into the bladder may result.

(6) As regards treatment, we have little doubt that antimony tartrate acts as a specific in this disease, but the amount required to effect a cure varies greatly, according to the amount of tissue destruction which has taken place. The amount in our cases ranged from 17½ to 179 grains. We wish to emphasise that the injections must be given in continuous series; interruptions in treatment are invariably followed by an extension of ulceration.

(7) In our opinion the higher organic compounds of antimony, such as Von Heyden 471, are even more efficacious and rapid in their action than is the potassium tartrate. (None of the solutions of antimony should be overheated by boiling.)

(8) The local application of antimony ointment in some cases is of distinct benefit. The ointment should be made in a strength of 1 per cent. antimony tartrate in white vaseline. The requisite amount of antimony tartrate is first dissolved in a small quantity of liquid paraffin. As a general rule, application of the ointment elicits pain, so that it may have to be made up in a weaker strength. The ointment must not be spread on to the healthy skin. As a general rule the ointment is left on the sore for two hours and then wiped off carefully, the sore washed with boracic solution, and dressed with boracic ointment. Alternation of dressing with eusol is often of benefit in those cases in which antimony ointment causes excessive irritation and pain.

There is some evidence that the administration of tablets of Thyroideum siccum, gr. v, at night, stimulates the growth of epithelium over the granulation surface.

In our experience it is doubtful if X-ray treatment gave any help.

Diagnosis.—The clinical diagnosis of ulcerating granuloma may be difficult, and at times impossible. In differential diagnosis one has to consider chancroid, primary syphiloma, and possibly primary carcinoma.

In chancroid the incubation period is usually less than one week, while a bubo is often an accompaniment. With chancroid there is never more than superficial ulceration. In this latter condition, by keeping the lesion clean and continuously applying dry sulphur, healing soon takes place, but in ulcerating granuloma such treatment has no effect.

Primary syphilitic chancre usually has an incubation period of three weeks or more. The base of the ulcer is usually indurated, the lymphatic glands are usually early involved and have the characteristic india-rubber feel; and examination of juice from the ulcer by a proper technique will reveal *Sp. pallida*. By the sixth week the blood is usually Wassermann positive, or becomes positive after arsenobenzol injection.

Carcinoma of the penis must not be forgotten. Here the age of the patient is a great help in diagnosis, as carcinoma is usually found in elderly people, and on the penis it often develops on the site of a former chancre. The typical induration and rolled edge of the lesion, with perhaps " shotty " glands sometimes painful, are usually sufficient for diagnostic purposes.

If doubt remains a section of the tissue must be made. In the absence of any demonstrable causative organism the diagnosis of ulcerating granuloma is made, clinically, on history of sore appearing after coitus in tropics; the distinctive depth, nature, and method of spread of the ulceration; the very red or reddish brown granulomatous base; and the penetrating offensive odour of the ichorous discharge.

These are characters sufficiently well marked to stamp themselves on the memory when once they have been critically observed and studied, and it is hoped that the illustrations in this paper will assist in the recognition of this lesion, and thus lead to the early institution of antimony treatment, the result of which is often striking enough in lesions which have resisted treatment, such as salvarsan, mercury and potassium iodide, to establish diagnosis. The test of the correctness, or otherwise, of diagnosis is based upon the reaction of the lesions to specific antimony therapeutic treatment; it must, however, at times be a prolonged test; for the effect of antimony on ulcerating granuloma pudendi is not always immediate.

It is questionable whether the condition described by McDonagh [11] as *ulcus molle serpiginosum* is not identical with *granuloma pudendi*. This *ulcus molle serpiginosum* is a chronic ulceration of the groin, usually appearing after infection with " soft sore," very resistant to local medication, but which responds to intravenous injections of antimony tartrate. This, and the fact that all McDonagh's cases, with the exception of two, had acquired their infection in the tropics, lend verisimilitude to this suggestion. Possibly some of these cases can be explained by a concomitant infection of soft sore with granuloma pudendi. Dr. Hanschell has permitted me to quote an instance of this kind, which occurred in his practice, and in which soft sores on the penis, acquired in the tropics, preceded by five months the appearance of deeply undermined ulceration in the right groin. This groin ulcer had been present and slowly spreading for nine months when it responded, almost immediately, to intravenous antimony tartrate injections. All other remedies failed. The soft sores were therefore only accidental precursors of a subsequently acquired *granuloma pudendi* (or *inguinale*).

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